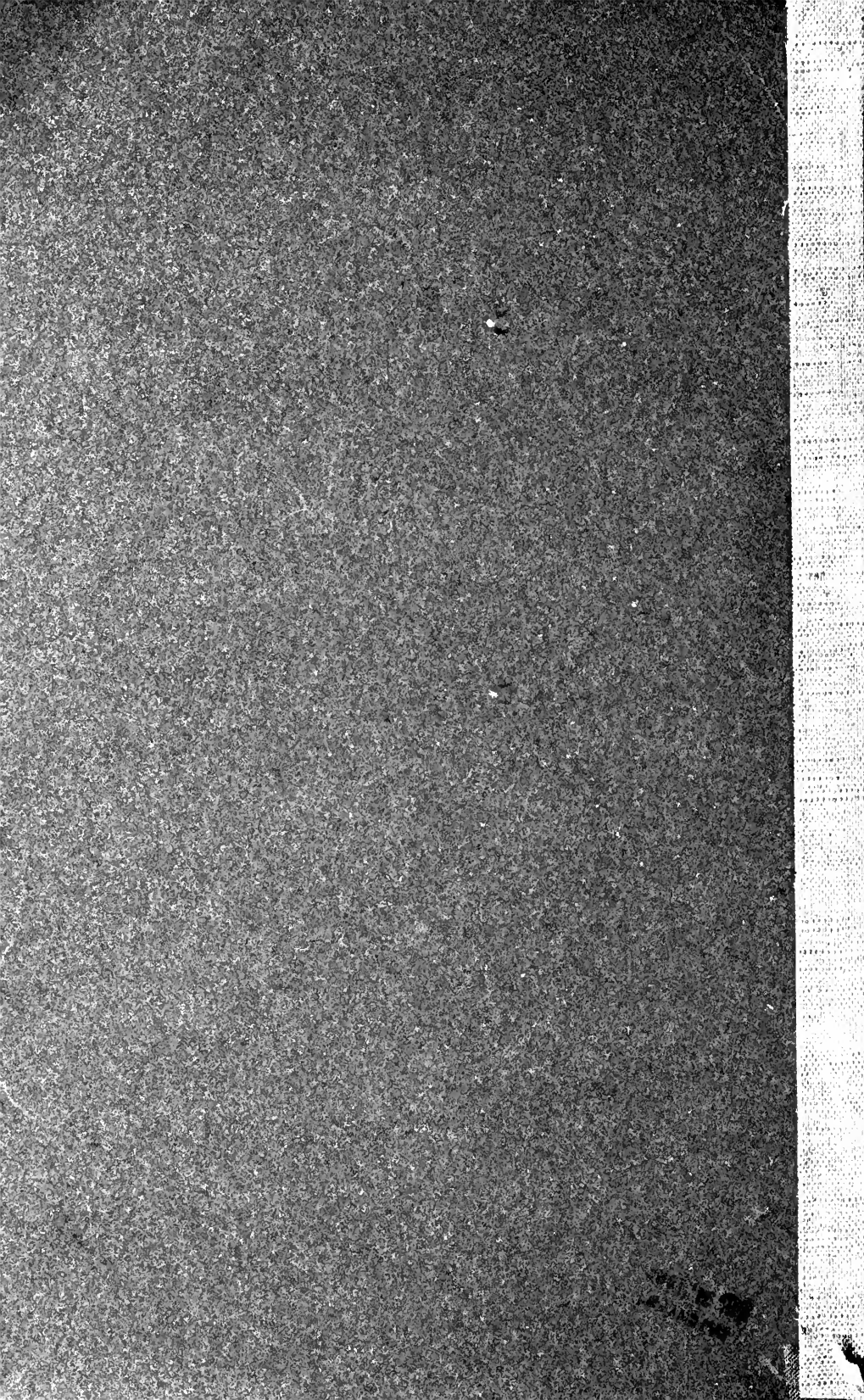


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TREASURY DEPARTMENT

Public Health and Marine-Hospital Service of the United States

no. 23

# PELLAGRA

A PRÉCIS

BY

PASSED ASSISTANT SURGEON C. H. LAVINDER

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PREPARED BY DIRECTION OF THE SURGEON-GENERAL

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WASHINGTON

GOVERNMENT PRINTING OFFICE

1908



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TREASURY DEPARTMENT,  
PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE,  
*Washington, July 24, 1908.*

The honorable SECRETARY OF THE TREASURY.

SIR: I have the honor to transmit herewith a brief manuscript on pellagra.

This interesting and highly fatal disease has but recently been discovered in the Southern States. It is a veritable scourge in certain portions of Europe and may become endemic in this country, as it is associated with the eating of diseased corn.

It is therefore of great importance, both from a public health and an economic standpoint, that knowledge of the disease be disseminated as soon as possible, and I respectfully request that the above-mentioned manuscript be published for distribution among health officers.

Respectfully,

WALTER WYMAN,  
*Surgeon-General.*

Approved.

L. A. COOLIDGE,  
*Acting Secretary.*



# PELLAGRA.

(MAÏDISMUS, PSYCHONEUROSIS MAÏDICA, AND A VARIETY OF OTHER NAMES.)

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By Passed Asst. Surg. C. H. LAVINDER.

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This paper is written with the purpose of supplying, in readily available form, some account of a disease which has been long known and studied, but knowledge of which is believed to be very infrequent among American physicians. Until of late years pellagra was unknown in the United States, and the literature on the subject in English is very meager and unsatisfactory. More or less recently, however, there has appeared in the Southern States a disease which is possibly true pellagra, and there is reason for believing that perhaps this disease may be quite prevalent, but unrecognized. Since it is of a serious nature, and epidemic in character, knowledge concerning it is becoming of much importance to the American physician, and more especially to the practitioner in the Southern States.

## HISTORICAL.

Pellagra has been known in Spain since 1735, and was first described by G. Casal, of Oviedo, who, observing the disease among the Asturian peasants and finding nothing on the subject in medical literature, called it *mal de la rosa* (from its characteristic erythema). He regarded it as a kind of leprosy. Later it was observed and described under a variety of names in Spanish literature.

It seems to have appeared in Italy about 1750, but was first described there in 1771, and Frapolli, of Milan, first applied the name of pellagra (Italian, pelle = skin, and agra = rough) to the disease. Here, as in Spain, the disease was described under several different names. By 1784 it seems to have become of such importance that a hospital was established under royal authority for a study of its nature, and the elder Strambio was placed in charge. About 1810 Marzari first called attention to the relation between maize and pellagra, and in 1844 Balardini first suggested the theory that the disease might be due to spoiled maize—that is, maize which had undergone change by reason of the growth of fungi on the grain.

From the greenish color produced by the parasites, Balardini's view was called the "verdet" theory. This theory has been developed and most ably defended by Lombroso.

In France early in the nineteenth century pellagra was first observed by the elder Hameau in the vicinity of Teste (whence the name, *maladie de la Teste*). In 1845 Théophile Roussel made a notable contribution to the study of the disease, and followed this later by others. He did much to clear up existing confusion, established the identity of pellagra with *mal de la rosa*, distinguished clearly pseudo-pellagra, and strongly advocated the "verdet" theory.

The disease appeared in Roumania early in the nineteenth century, and a good deal of valuable literature has followed. The work of Babes should be mentioned. Sandwith has reported the disease from Egypt, and many other observers have noted it in various parts of the world, usually in sporadic form.

#### GEOGRAPHICAL DISTRIBUTION AND STATISTICS.

At present pellagra is most prevalent in northern and central Italy and in Roumania. It is also found in parts of France, but of recent years, since other cereals have replaced maize, it has much decreased. It is still prevalent in parts of Spain, also endemic in Corfu, and occurs rather extensively in Upper Egypt. It is likewise often reported from Asia Minor, Austria, Servia, Bulgaria, and some other parts of southern Europe, as well as occasionally from India, Africa, Barbados, Mexico, South America, and lately the southern United States.

The disease has been, and still is, a veritable scourge to certain parts of Europe. It seems to have followed close upon the introduction of maize culture from America, first in Spain in 1700, and later in other parts of Europe. The original homes of maize (America and Asia) have, however, escaped, probably by reason of climates better adapted to maize culture.

The pellagra zone is but a small one when compared with the area over which maize is cultivated, yet pellagra does not occur except where maize is grown and extensively used as food by the poorer classes.

Authors have given as geographical limits of endemic pellagra 42° to 46° north latitude, 11° west and 26° east longitude of Paris, but these limits would have to be extended to include Egypt and Corfu.

Without quoting full data, some idea of the extent of the disease may be gained from the figures which follow: Triller (<sup>1</sup>) states that there are (1906) 30,000 pellagrins in Roumania; that in certain parts of Italy as much as 30 per cent to 50 per cent of the population have the disease; and that in 1899 there were nearly 73,000 sick with the dis-

ease in all Italy, this being upward of 10 per 1,000 of the rural population. Tuczek (<sup>2</sup>) states (1893) that in Spain 2 per cent of the rural population are affected; that in 1884 there were 10,000 pellagrins in Italian hospitals and insane asylums. He also says that about 10 per cent of the pellagrins in Italy are mentally affected. Sandwith (<sup>3</sup>) states that he has seen over 500 cases in the five years from 1893-1898 in his wards at the Kasr el Ainy Hospital at Cairo. The disease was not reported in Egypt till 1893.

More recent figures would show no amelioration of these conditions. There were said to be in 1907 about 100,000 pellagrins in Italy, and upward of 50,000 in Roumania.

#### ETIOLOGY.

It is the accepted opinion of most students of the disease that pellagra is an intoxication due to using as food Indian corn (maize), which, under the influence of unidentified parasitic growths (fungi), has undergone certain changes with the production of one or more toxic substances of a chemical nature. The relation between Indian corn and pellagra was noted as long ago as early in the nineteenth century, and about the middle of the century Balardini first put forward his "verdet" theory, already noted above.

Alcoholic and watery extracts have been made from spoiled maize, and chemical substances of an undetermined nature have also been isolated from the same source. Lombroso has done some notable work along this line, and he, with others, has given these extracts, etc., to both men and animals with the production of symptoms analogous to pellagra in a greater or less degree, and in animals, at times, with suggestive post-mortem lesions. Lombroso applied the name "pellagrozein" to one extractive made by him.

All such work is as yet, however, in an undetermined state, and no definite statements can now be made as to the chemical nature of the toxic substance or substances involved. With regard to the parasites found on maize it may be said that the varieties are numerous, and no single one seems to be constant enough to be rated as the definite causative agent. So far as the causal relation existing between spoiled maize and pellagra is concerned, students of pellagra seem generally to be in accord, but it must not be overlooked that this relation is by no means definitely understood.

It might be mentioned here as of much interest that Babes (<sup>5</sup>) and other workers have shown that there exists in the blood of pellagrins a substance which is antagonistic to the toxic action of extracts made from spoiled maize (antitoxic substance).

There are other views as to the nature of pellagra not so widely accepted. Of importance might be mentioned the following: auto-intoxication, the view that a constant and almost exclusive diet of

corn produces certain changes in the vegetating properties of the intestinal flora with the production of poisonous substances in the bowel; and the somewhat similar view that the disease is an intestinal mycosis, the offending micro-organisms being eaten with the corn and colonizing in the intestinal tract; some observers regard the disease as of an infectious nature, and several workers have reported isolating bacteria from the blood and organs, but as yet without confirmation; then there is the idea that pellagra is not a definite morbid entity at all, but only a symptom complex sometimes observed in alcoholics and in cachectic states of diverse origin, the erythema being regarded as only a common, solar erythema; the food value of maize has been questioned by some, and the suggestion made that pellagra is but a form of starvation. It seems well established, however, that good maize is extremely nutritious, and is richer in albuminoids than any other cereal when it is matured and dried.

The disease generally occurs among the poorer classes of the rural population who subsist largely, or exclusively, on corn, most usually prepared by boiling corn meal in salt water (called "polenta" in Italy). Observation also shows that in pellagrous countries the corn is often of a poor quality, gathered before maturity and not properly cured and stored, so that parasites more easily develop upon it.

Among predisposing causes are usually given:

*Seasons, heat, and sun.*—The appearance, or recurrence, of the symptoms of the disease in spring is almost constant, but the seasons, heat, and sun are thought to have only indirect effects in the maturing of corn and development of parasitic growths; the actinic rays of the sun probably often act as an exciting cause in the production of the erythema.

*Climate* seems to have no effect beyond the indirect influence in growing and maturing maize and the development of parasites on the grain.

*Sex* seems to exert no influence, though nervous symptoms are said to be more dominant in females.

*Age.*—The statements are somewhat discordant, but most authors agree that the disease does not occur in infants unless they are fed on spoiled maize. It seems to occur more frequently between about the ages of 20 to 40 years.

*Alcoholism, previous sickness, constitution, hygienic conditions, poverty, venereal excesses, depression, etc.*—These all exert only the indirect influence of lessening resistance. It should be added, however, that several observers believe that alcohol distilled from spoiled maize may contain the pellagrogenous poison.

*Other associated diseases.*—It should be noted that such parasitic diseases as anchylostomiasis (uncinariasis) and bilharziosis are frequently present in pellagrins. Malaria, too, is common. These are,

however, regarded only as complications, and not as causative agents. They frequently obscure the clinical picture of the disease, however.

*Nationality and occupation* seem to have no effect. The disease is limited to certain countries only because of the poor quality of the corn and its consequent readiness to undergo the change described. The poor rural population suffer most because they live largely, if not exclusively, on corn and usually of the poorest quality.

*Heredity*.—The disease is not hereditary, but the children of generations of pellagrins are feeble in resistance, and of lowered physical vitality.

*Contagion*.—The disease is not contagious, and the sick may associate intimately and freely with the well, and if spoiled maize is not eaten the disease does not occur.

#### PATHOLOGIC ANATOMY.

The morbid anatomy is neither constant nor characteristic. In a disease presenting such a variety of symptoms and characterized by such great chronicity, with the frequent presence of intercurrent affections and senile evolutionary changes, one could hardly expect to find a definite, single, morbid condition, and must learn to discriminate the manifold, accidental changes so frequently found.

Tuczek (2) describes as part appearances of cachexia the following: wasting of adipose and muscular tissues, brittleness of the bones (*fragilitas ossium*), atrophy and fatty degenerations of the internal organs (chiefly those innervated by the vagus), heart, kidneys, spleen, intestines, liver, and lungs.

He also describes three further groups of morbid changes: (1) intestinal: atrophy of muscular coat, with occasional hyperemia and ulceration of the lower part of the tract; (2) abnormal pigmentation (similar to senile change), especially of ganglionic cells, heart musculature (brown atrophy), hepatic cells, and spleen; (3) alterations in the nervous system. The variously described conditions of hyperemia, anemia, edema, and at times inflammatory affections of the central nervous system and its coverings, together with the obliteration of the central canal of the cord, he regards as not peculiar to pellagra, but as accompanying conditions present in many chronic affections of the central nervous system and in senility.

The findings in the brain are in most cases negative except for occasional fatty degeneration or calcification of the intima of small blood vessels and pigmentation in the adventitial coats. In cases where a long-continued psychosis has led to a high degree of imbecility atrophy of the cerebrum may be found. In the cord the changes are fairly constant and important; degenerations in the lateral columns in the dorsal region, and in the posterior columns in the cervical and dorsal regions; very few changes are found in the lumbar cord.

He also states that typhoid pellagra has no special pathology.

With regard to degenerative changes in the peripheral nerves, he thinks such changes should be viewed with caution, when one considers their great frequency in chronic illness of many kinds.

Lombroso (<sup>4</sup>), from observations on 113 necropsies, describes changes very similar to the above. He states, however, that he has found also degenerative changes in the posterior roots of the spinal cord. He says that in the most typical cases, the spinal cord lesions remind one of incipient tabes, except that few changes are found below the dorsal region, whereas in tabes the lumbar region is chiefly affected. In both diseases, however, a combination sclerosis is present.

Marie (<sup>5</sup>) points out that Lissauer's zone and Clarke's column are involved in tabes, but not in pellagra, and thinks the changes found in pellagra have a greater resemblance to those of dementia paralytica.

Radcliffe-Crocker (<sup>6</sup>) has described the skin changes as consisting of, first, congestion; second, thickening and pigmentation; and third, atrophic thinning.

#### PATHOGENESIS.

Procopiu (<sup>7</sup>) points out that pellagra is an intoxication disease of great chronicity; that the greatest force of the poison is expended on the nervous system; that our lack of knowledge as to the chemical nature of the poison or poisons involved leaves us in great doubt as to the mode of action, length of stay in the body, and method of elimination.

He suggests that perhaps elimination may take place from the skin and mucous membranes, giving rise to the exanthem (erythema) and the enanthem (stomatitis and intestinal hyperemia), though the possible dependence of these symptoms on the nervous system is not to be overlooked (tropho-neurotic). He also suggests that the great chronicity of the disease and the slow progress to recovery, when this takes place, gives rise to the thought that the poison or poisons may be very slowly absorbed and equally as slowly eliminated.

Perhaps it should also be noted that the question has been discussed as to whether we must regard the disease as a chronic disease with periodic recurrent manifestations (exacerbations), regardless of a continuously acting cause, or whether it is simply a question of recurrent re-poisoning. The nature of the disease and the weight of authority seem to support the former view.

#### SYMPTOMATOLOGY.

Pellagra is both an endemic and epidemic disease, which occurs in those who feed on spoiled maize, and is characterized by an erythema of the skin, digestive disturbances, and nervous disturbances. It may terminate in such serious conditions as grave cachexia or insanity;

it is periodic in its manifestations, and usually appears with the beginning of spring, ameliorates during summer, and ordinarily in winter the symptoms disappear to such an extent as often to give the false idea of recovery. So long as the cause persists, however, it reappears each year.

The disease usually begins with gastro-intestinal disturbances, followed shortly by the erythema of the skin, and in a brief while there is more or less involvement of the nervous system. It is a slowly advancing toxemia, the brunt of which, in the end, is borne by the nervous system, and each annual recurrence leaves a deeper and more indelible mark on the mental and nervous condition of the sufferer.

The symptoms are divided by most authors into three periods or stages. Many other divisions have been suggested. None seem entirely satisfactory. The division into three stages, while artificial, is convenient and is generally adopted. Such a division has no reference to the length of time the malady has existed, but is based largely on the intensity of existing symptoms. A patient may have suffered from pellagra for many years and still remain in the first stage of the disease; whereas another, in a much briefer period, may advance to the third stage. The disease is essentially chronic, although an acute (or florid) type is usually mentioned by writers on pellagra. Small space seems to be devoted to any description of acute types, however, and one is left to infer that the acute disease does not differ in symptomatology from the chronic, but that it is simply far more rapid in its evolution.

#### FIRST STAGE.

Prodromal symptoms are said not infrequently to be present, but since the disease occurs largely in the peasant class, who are inured to the hardships of life and pay small attention to minor ills, this stage of the disease is not often observed. The prodromes are stated to be lassitude, vertigo, headache, general malaise, and perhaps mild digestive disturbances.

Pellagra, as stated, manifests itself in early springtime, as a rule. There is a sensation of a heat in the mouth and stomach, taste is altered, appetite usually lost, and often pyalism is present. The tongue is coated, and an examination of the mouth often shows redness of the mucous membrane, with vesiculation, or even superficial ulceration. Dyspeptic symptoms, with flatulency, are noted, and sometimes abdominal pain (usually epigastric); occasional vomiting may occur, especially in alcoholics; diarrhea is often present—at times constipation—and the diarrhea, as well as the vomiting, may in some cases be of a spasmodic type; sometimes it is dysenteric in character, muco-sanguinolent, with colic and tenesmus.

In a short time the characteristic erythema appears, selecting nearly always the uncovered parts of the body, and being symmetrical in its distribution. Its appearance is usually accompanied by a sensation of heat and swelling, with itching, in the affected parts.

Muscular weakness, especially of the lower extremities, is usually evident early, and patients tire very easily.

The temperature is usually normal, though there may be a slight evening rise. If there is much fever, complications should be sought for. Pellagra is described as a feverless disease. The pulse may be accelerated, though at times slow. Functional heart murmurs may occur, but should be sought later.

Vertigo is often present and very annoying; headache, usually occipital, is frequent, and often severe; rebellious insomnia occurs; various neuralgias are not seldom in evidence, and especial stress is laid by some on spinal neuralgias, with cramp-like pains extending to the extremities. The knee jerks at this stage may be exaggerated.

Intelligence, even at this early period, is often affected, and there is mild mental weakness with depression of spirits. Pellagrous children wear a serious face and appear old.

Ocular phenomena are sometimes present, inequality of pupils occasionally, dilatation often. Diplopia and amblyopia may occur. Cataracts are in some sections frequent, both in adults and children. Inflammatory and atrophic alterations are rarely observed.

The blood changes, beyond a frequent, mild, secondary anemia, are unimportant.

The urine often shows no important changes. Albuminuria is not very rare, and when it occurs there is generally an associated nephritis. This nephritis usually occurs, however, toward the end of the disease. The diazo reaction is not seldom met with.

#### SECOND STAGE.

While erythema, digestive, and some nervous disturbances characterize the first stage, the second is marked by an aggravation of all of these symptoms and the appearance of new and marked evidences of involvement of the nervous system which now dominate the scene.

The anemia increases, loss of weight is apparent, greater physical weakness appears, the skin of the erythematous patches becomes thickened and covered with a hard, cracked, pigmented epidermis, sometimes of a yellowish color.

The stomatitis is aggravated, ulcerations are more frequent and, if not before, the tongue becomes now smooth and denuded of epithelium—the "bald tongue."

The diarrhea grows more persistent, sometimes sanguinolent, at other times, and more often, it is serous. This serous diarrhea is not

seldom painless and very persistent. If continued, it leads to the third stage of cachexia.

The nervous phenomena are much exaggerated, and the great characteristics of this stage are the severe cerebro-spinal disturbances.

Vertigo becomes more grave and prominent. Headache occurs with a sensation of weight, and insomnia; neuralgias are more frequent and severe; psychical manifestations are seldom lacking and have usually the character of melancholia; in light cases there may be simply a mental feebleness, slow cerebration, with mild irritable depression, and aversion to any activity. This may develop into stupor. In severe cases there exists melancholia with anxiety, delusions of persecution, and disturbed ideas on religious matters. Refusal of food and suicidal tendencies are common. Maniacal attacks with homicidal tendencies are less frequent. Melancholia may end in dementia. Defects of consciousness occur and delirium of a melancholic character. The circular type of insanity as well as paranoia are said at times to be observed.

Muscular feebleness is marked and partial paralyses may occur, or even paraplegia and hemiplegia have been described. States resembling tetany may be seen sometimes, with paroxysmal-like, painful, tonic contractions in the lower extremities; and there may occur in those cases contractures of the upper and lower extremities in the half-flexed position.

The gait is usually paralytic, occasionally paralytic-spastic; never, it seems, ataxic.

Tremor of the upper extremities, head, and tongue are recorded in many cases.

The electric muscular irritability seems to show no constant deviation from the normal.

Epileptiform seizures may occur, but definite attacks with loss of consciousness are very rare. More frequently it resembles cortical epilepsy, cramps in single limbs, short pauses in consciousness, and vertiginous spells.

The skin sensibility seems to be irregular and of not great importance. Various paresthesias are frequently present.

The ocular phenomena already described may more likely occur in this stage.

The skin reflexes are as a rule normal. The tendon reflexes usually show deviation from the normal, but are often irregular. In some cases they are normal, in most increased, sometimes weakened or lacking altogether. Differences in the upper and lower extremities and in the two sides are recorded.

Vaso-motor and trophic disturbances, besides the erythema, are often noted in the skin, such as general paleness, *cutis anserina*, cold sensations, and the like. Edema also occurs, and capillary injections about the face.

## THIRD STAGE.

This is really the terminal stage and is chiefly characterized by cachexia. The symptoms already described do not give place to new ones, but, on the contrary, they are present and aggravated. The cachexia now, however, stands boldly in the foreground, with dementia, paralyses, and other cerebro-spinal phenomena still prominent in the picture.

There is an increasing marasmus, with marked anemia, atrophy of subcutaneous fat and musculature, and a lack of resistance against intercurrent diseases. In addition there are great muscular feebleness, perhaps paralyses, including the bladder, and an uncontrollable, painless, serous diarrhea. Death follows, with the signs of heart weakness and its consequences, edema, and effusions; or some intercurrent disease, such as acute tuberculosis of lungs, which is common at this period, or septicemia following decubitus, may close the scene.

## TYPHOID PELLAGRA.

At this stage not infrequently the fatal termination may take place in what is called typhoid pellagra (*typhus pellagrosus*).

It is to be understood that this is not true typhoid, although this may at times be a complication of pellagra. Eberth's bacillus is not present and the morbid lesions show nothing characteristic. It should also be noted that nearly all authors seem to agree that this is not acute pellagra, and never occurs except at the termination of chronic cases.

The condition is described as one of profound prostration, dorsal decubitus, dry tongue, fetid breath, continuous fever, feeble, small, perhaps irregular pulse, and frequent bed sores.

The psychical condition becomes usually one of delirium, or perhaps partial stupor.

There is, in addition, a marked, general neuro-muscular irritability. The whole musculature is held in a condition of rigidity, almost to the extent of tonic contraction. In spontaneous motion there is a perceptible tremor and a suggestion of incoördination. Speech is drawling, trembling, frequently of a nasal quality. The head, through contraction of the neck muscles, is drawn backward, and now and then raised and moved convulsively from side to side. The facial expression is anxious and the facial muscles move with a tremor or fibrillary contractions.

The lower extremities are found in a strong condition of extension, with plantar flexion of feet. The tendon reflexes are increased and a simple percussion of the patellar tendon may result in a diffuse clonus of the entire limb, accompanied, perhaps, by a spasm of the whole body.

There may also be present hyperesthesia and increased reflex irritability of all the sensory areas.

Pellagra is described as a feverless disease, but in this state the fever is constant and often high.

Roseola is lacking.

In most cases death occurs in one or more weeks, often in a terminal bronchitis.

#### THE PELLAGROUS ERYTHEMA.

The erythema is the characteristic symptom of the disease. It makes its appearance almost invariably in the springtime, develops during the summer, and fades with the appearance of winter. It appears symmetrically and on the uncovered parts, selecting at first especially the extensor surfaces, backs of hands and forearms, face, back of neck, upper chest, and dorsal surfaces of feet. Later the flexor surfaces become involved, but the palmar and plantar surfaces always escape. Cases have, however, been described when the erythema involved the covered parts of the body or was, indeed, generalized.

Its relation to the sun's rays has been a subject of much discussion, but the most generally accepted idea is that the actinic rays of the sun simply act as an exciting cause in persons already victims of the disease.

It usually makes its first appearance on the backs of the hands, developing later in other places. The skin in the beginning becomes red with sensations of burning and itching, and usually some puffiness is observed—all very similar in appearance to a marked sunburn. This red color disappears on pressure, but promptly returns when pressure is released. After some days bullæ may appear, and these may fuse into large plaques filled with serum or even sero-purulent or sanguinolent fluid. The edema may then disappear, the epidermis dries and falls in small, grayish scales.

At other times the epidermis, after the initial redness described, may take on a dark color, described as brownish or blackish, chocolate colored, or plum colored, after which it dries and scales with no bullous formation.

Desquamation without erythema has been reported; also pustular erythema, especially on the face. Among some, exfoliation may occur in large flakes.

After the first attack the skin remains pigmented for some time, and as repeated attacks occur it gradually undergoes chronic thickening with pigmentation, often of a dirty yellow, yellowish green, or bronzed color. The skin is then indurated, thickened, hard, and rough. Later its elasticity partially disappears, the articular folds grow deeper, painful fissures and thick crusts may develop, or even

small ulcerations after exfoliation. Ecchymotic spots may sometimes be seen.

After repeated attacks the skin may become atrophic, thin, and parchment like, with almost entire loss of elasticity and show whitish spots like the *striae gravidarum*. When compared with the skin of the rest of the body the difference is then striking.

It is to be noted that cases are described in which the erythema is wanting—*pellagra sine pellagra*. It seems, however, to be the general opinion that the absence of this symptom is only temporary, and that its final appearance can be looked for in all cases. Without the erythema diagnosis is difficult and must often remain doubtful.

#### PELLAGROUS INSANITY.

In a few words, pellagrous insanity seems usually to be of the melancholic type. Acute maniacal spells may occur, however, with homicidal and suicidal impulses. Suicide by drowning is especially noted among the pellagrous insane.

The general characteristics, otherwise, of pellagrous insanity seem not to differ greatly from those of other insanities.

The diagnosis is to be made from the history and the coincidence of other symptoms.

Recovery may take place, but in advanced cases the outlook is poor, and even if recovery take place there is left permanent mental deterioration.

#### FORMS OF PELLAGRA.

Many forms have been described and various divisions made. One or more symptoms may dominate the picture and so permit of artificial classifications.

Procopin (7) gives the following classification:

1. Gastro-intestinal.
2. Nervous, with mania.
3. Nervous, with paralysis (pellagrous myelitis).
4. *Pellagra sine pellagra*.
5. Typhoid pellagra (not a very definite type; rather a complication).

#### DURATION.

As stated, the manifestations are periodic and usually appear in the spring. If the winter is warm they may appear earlier. The erythema is usually preceded by other symptoms.

The duration of the disease is indeterminate and there is no regularity about the succession of the various stages. A pellagrin may be very ill one year and suffer lightly the next. The disease, in some, may remain stationary in the first stage for as much as twenty

years, while in others it may reach the second, or even the third, in the first or second attack.

Development seems to be more rapid and grave in children.

#### FALSE PELLAGRAS.

In the literature of pellagra, one is constantly reminded that there is a false or pseudo-pellagra which must be carefully discriminated from the true disease.

Roussel seems to have first pointed out the fact that many cases were being called pellagra which on careful analysis could not be so classed. In short, it appears that pseudo-pellagra is simply not pellagra at all, and is some other disease with a wrong diagnosis.

Alcoholics, with peripheral neuritis, and cases of dementia and general paralysis in asylums seem at times to cause confusion. Solar erythemas also are mentioned. And in cachexias of diverse origin, some pellagrous symptoms may at times appear.

This question does not, however, appear to be so simple a matter as many authors assert. For example, Manson<sup>(8)</sup> says:

The disease is pellagra when it fits in with the orthodox theory and when it can be connected in any way with maize; but when this is not possible, the disease becomes pseudo-pellagra.

In this connection, one might also consult Cecconi's<sup>(9)</sup> thesis.

#### DIAGNOSIS.

The diagnosis must depend on the presence of the characteristic triad of symptoms—erythema, digestive, and nervous disturbances. *Pellagra sine pellagra* will offer difficulties.

In the differential diagnosis, various diseases are mentioned:

Other grain poisonings, as ergotism and lathyrism, must be distinguished by the history and difference in symptomatology.

Scurvy, leprosy, and beriberi are also spoken of, but, it seems, should be easily differentiated.

Lichen, eczema, and other similar skin lesions are wanting in the constitutional symptomatology.

Chronic mercurial and arsenical poisoning can be differentiated by the history, symptoms, and development.

Various food poisonings must be discriminated by the history of the case and the usual more rapid development, with the omission of characteristic pellagrous symptoms.

Acrodynia is rare and the character and distribution of the exanthem are said to be quite different.

When the subjective symptoms are prominent, confusion with a functional neurosis seems to be possible.

Difficulty may occur because of the resemblance to dementia paralytica. The lack of speech disturbance and nonprogressive course will here aid in differentiation.

Typhoid pellagra might be confused with an infectious disease, or uremia, or perhaps diabetic coma. The typical fever course, negative condition of internal organs, character of urine, and the absence of an acute exanthem must here be taken into consideration.

#### PROGNOSIS.

Usually serious, but it is dependent on the stage of the malady and the opportunity of placing the sick on better food and under better hygienic conditions.

In the first stage, recovery is said to be easily secured; in the second stage it is more difficult, and intelligence may remain permanently enfeebled; in the third stage death is the rule. Recovery may occur from typhoid pellagra, but it is very rare.

A recurrence of the disease is inevitable if the cause persists.

The great gravity and danger of the disease lies in the number of people affected, and in its immediate and remote consequences not only to the individual, but to the race—intellectual feebleness, lessened resistance, economic loss, physical deterioration of the race, etc.

#### TREATMENT.

The treatment naturally divides itself into prophylactic and medical.

*Prophylaxis.*—This may be summed up briefly—cease using spoiled maize as food. This seems simple enough, but in reality is often difficult of accomplishment for many obvious reasons. In individual cases it may often be easy, but to apply it to a large area of territory is another matter. The only apparent methods would seem to be: (1) avoid alterations in maize and consequent feeding on a toxic substance; (2) replace maize with some other cereal and cease using all food and drink derived from maize.

Many and various attempts have been made in Italy to do the former by the establishment of drying ovens, economical kitchens, pellagrous hospitals, etc., but such efforts have not met with great success. As for the latter, at present the difficulties seem almost insuperable.

*Medical.*—Here all we can do is to remove the cause and treat the symptoms. The treatment, it is needless to add, is often unsatisfactory.

Good, easily assimilable food is recommended with a general tonic regimen. The diet is a matter of importance.

Among drugs arsenic, quinine, strychnine, and iron are all advocated in various forms. Opium is recommended for the diarrhea.

Systematic purgation is discouraged. Internal antiseptics are said to be useless. Salt solution subcutaneously has been recommended at certain stages. Salt frictions and various baths are said to be of service. More or less recently atoxyl has been highly recommended.

So far as local treatment of the skin is concerned, any bland ointment, such as zinc oxide, may be used, but the treatment is said to be of little benefit.

#### PELLAGRA IN THE UNITED STATES.

The culture of maize in the United States has been practiced since before the discovery of America, and it has always been a staple article of diet over a large area of territory, yet, with the exception of a few sporadic cases in Mexico and Central America, the North American continent has been singularly free from the disease. This has been attributed by writers on pellagra to a climate well adapted to growing maize, and probably to better general hygienic conditions among the poorer rural classes.

Exclusive of Sherwell's <sup>(10)</sup> note on a case of pellagra seen in a sailor aboard ship in New York in 1902, the first case of the disease in the United States was reported by Harris, <sup>(11)</sup> of Georgia, in 1902. He reported one case presenting the classic symptoms of the disease and thought it possibly true pellagra.

Searcy, <sup>(12)</sup> of Alabama, in 1907 described an epidemic of pellagra occurring in the Mount Vernon Insane Hospital (for the colored insane of Alabama). There were 88 cases and 57 deaths. He states that a few cases of such a disease had been noted there as long ago as 1901, but that their real nature was unrecognized. He also states that after attention was called to the disease some cases were recognized in the hospital for the insane at Tuscaloosa.

His cases generally ran a more or less acute course, and the mortality was very high (about 64 per cent). He, with McCafferty and Somerville, of Alabama, and Dyer, of New Orleans, regarded the disease as pellagra.

Since his report Merrill <sup>(13)</sup> has recorded a sporadic case seen in Texas.

More recently in a report made to the South Carolina board of health <sup>(14)</sup> by the medical members of the board of regents and the medical staff of the state hospital for the insane several cases of a similar disease are described, and the opinion is expressed that while a pellagroid disease is undoubtedly present in South Carolina, it remains to be proved whether it is the true pellagra of the Old World, the observations being too few for a final opinion. Marked attention is also directed to the frequent presence of hook worms. This report also makes reference to the report of the Alabama hospitals on the matter, but I have been unable to see this.

Still more recently, at the last session of the American Medical Association in Chicago in June, 1908, R. H. Bellamy, of Wilmington, N. C., read a paper on pellagra in North Carolina (not yet published), and a few days later, at the meeting of the North Carolina Medical Society, papers on the same subject were read by Wood and McCampbell, of North Carolina, and by myself, and a discussion followed (all as yet unpublished). In these papers were reported a number of cases of a disease similar to that already described in the southern United States.

An analysis of these various reports would seem definitely to show that probably for the past several years there have occurred in the southern United States sporadic cases of an unrecognized nature resembling pellagra; that more recently (within the last one or two years), for some reason or reasons unknown, this disease has rapidly increased in numbers and extent of territory involved; that the disease as observed bears a close resemblance to the accepted description of pellagra as it occurs in the Old World, though different in some particulars; and, finally, that the acute cases greatly preponderate and the mortality is high. It may be added that while some doubts have been expressed, as is natural among men inexperienced in pellagra, yet there is a very general opinion that the disease in question is in all probability true pellagra.

If the cause of pellagra be accepted as feeding on spoiled maize, then the maize crop of the United States must in recent years have undergone decided change in some respect, for maize has always been very extensively used as food in the southern United States, and pellagra has not appeared in former years. This is a subject which will require extensive investigation should the disease continue to advance.

So far as the symptomatology of this disease is concerned, it follows in general lines that already described above, and only the variations need be noted.

The most notable thing to be remarked in comparing these cases with the descriptions of true pellagra is, as stated, the great preponderance of acute types and the high mortality. Acute cases in the Old World do not seem so frequent, and great chronicity characterizes the disease there.

Of the cases described elsewhere in the South and more especially those occurring in Wilmington, N. C., and its vicinity, several of which I have had the opportunity of seeing, the disease, with its triad of symptoms—erythema, digestive, and nervous disturbances—develops rapidly: its symptoms are severe, and the fatal termination is often but a matter of a few days, or, at most, a few weeks. There is frequently severe stomatitis and diarrhea, a marked and persistent erythema,

mental dullness, even stupor, and frequent delirium, rapid emaciation, with a low grade of fever, and too often comparatively early death.

The chronic types are, however, seen too with their slow, though steady, advance, but even these do not seem to possess the great chronicity described in the pellagra of the Old World.

One other variation is the divergence in many cases from the strict seasonal recurrence of the manifestations of the disease. It observes more or less generally a seasonal recurrence, but not with the strict regularity described for Old World pellagra.

It may be added that among the cases seen at Wilmington, N. C., nephritis has not been infrequent, and that indican has been often found abundantly in the urine. Of the parasitic diseases, malaria has been observed occasionally, round worms once, but not uncinariasis, so far as I can learn.

It might also be said that variations of this character are not sufficient to discredit the diagnosis of pellagra. It is a disease of varied symptomatology. For example, Kaposi<sup>(15)</sup> says:

The symptoms of pellagra have been described in various ways. I believe this is owing to the fact that the disease does really occur in various forms, may run a more acute or an extremely slow course, and may exhibit very few or very many symptoms.

Whether this disease be true pellagra or not, it has so far proven itself a factor to be reckoned with in some of the Southern States, and it should receive now the most earnest attention and careful study of those medical men under whose observation and care such cases may chance to fall. This will in all likelihood be the especial province of the southern physician.

In conclusion I desire to express my thanks to certain local practitioners at Wilmington, N. C. To Dr. Thomas M. Green I am indebted for the privilege of seeing a case of the disease; to Dr. R. H. Bellamy I am indebted for many favors; and to Dr. E. J. Wood I am especially indebted. I have had the privilege of seeing and studying several of his cases, and with him have reviewed much literature and done a good deal of other work.

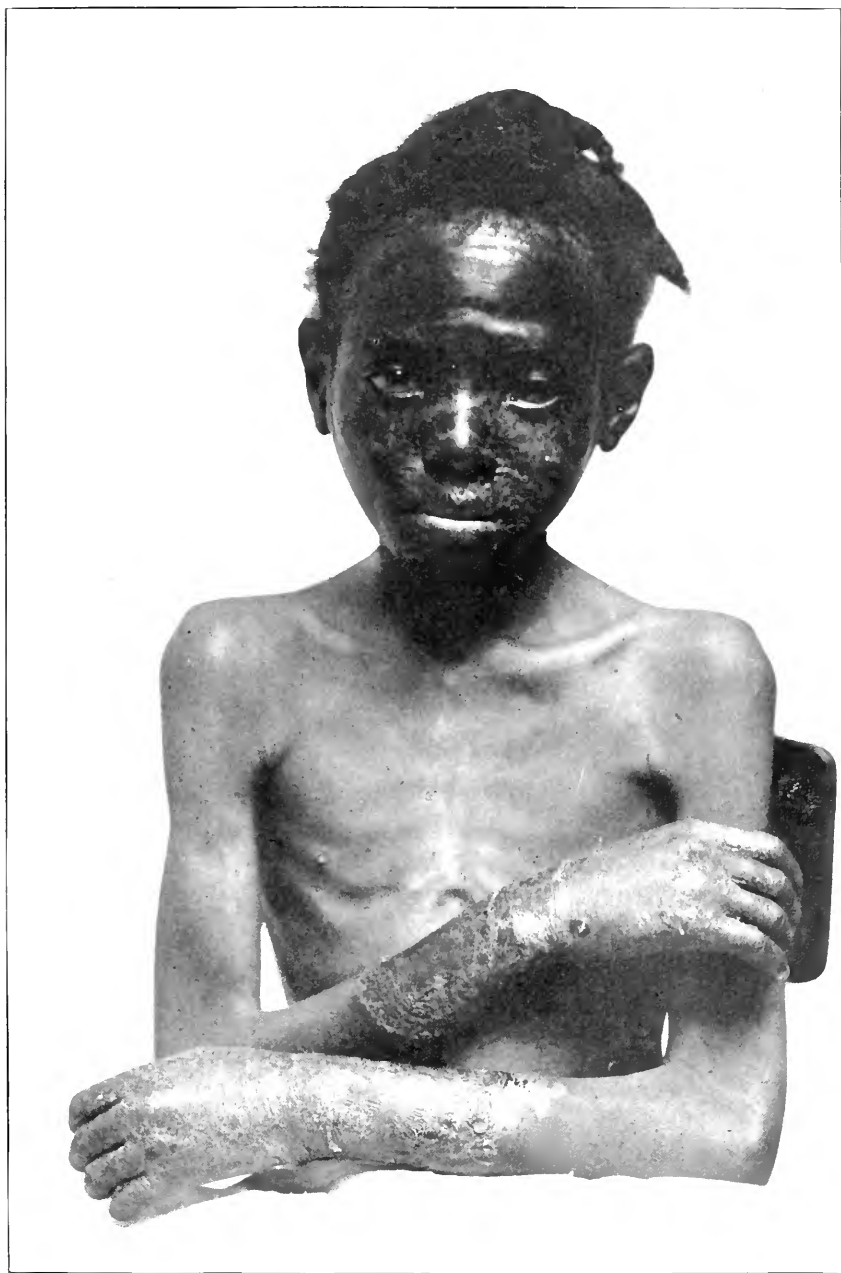
For most of this précis I am under obligations to some of the well-known literature of pellagra, of which, as is very evident, I have made extensive use. I have, as far as possible, purposely refrained from *verbatim* quotation in order not to interrupt the continuity of a paper of this kind. I have tried in the appended brief bibliography to make some acknowledgment of my indebtedness. I am also under obligation to the librarian of the Surgeon-General's Office at Washington for information and many courtesies.

## BIBLIOGRAPHY.

The literature of pellagra is extensive, and in the Index-Catalogue of the Surgeon-General's Library, at Washington (Vol. XII, new series), the list of titles will be found to reach the length of some 8 or 9 pages.

Most of the literature is in Italian, French, or German. There is but little in English. The writings of Roussel and Lombroso are important. The monographs of Tuczek and Procopiu are more recent and give a good account of the disease. I am especially indebted to these two authors. Sandwith's article, in English, is brief, but gives a good account of the disease in Egypt. Most of the dictionaries, encyclopedias, and reference handbooks give good brief articles. In Allbut's System of Medicine, edition of 1905, will be found a fairly satisfactory account. In most of the larger text-books on the skin will also be found some description of the disease.

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DR. E. J. WOOD'S CASE.

Female, age 11 years, an acute type, with death about four months after the appearance of the first symptoms; also had the erythema on the back of neck, and shortly before death it appeared on the dorsal surfaces of the feet. This case had a younger sister who presented first symptoms at the same time, but she recovered.













